

REMARKS

Prior to this amendment Claims 16-48 were pending. Claims 16-19, 23-26 and 40-45 and 48 are withdrawn as drawn to a non-elected invention. Claims 20, 27, 28, 32, -35, 38, 39, and 46 are amended. Claims 20, 28, 32, -35, 38, 39, and 46 are amended for proper dependency. No new matter is added by way of this amendment. Claim 27 is amended for technical clarity. Support is found at p. 48, lines 16-20, and p. 50, lines 17-20, of the application as filed. Applicants submit that no new matter is introduced by way of this amendment. Applicants respectfully request entry of this amendment as it puts the claims in condition for allowance or better condition for appeal.

I. Interview

Applicants appreciate the Examiner's telephonic interview of July 12, 2004. Applicant's representative and the Examiner discussed the cited reference Pinkel (US Patent 5,837,196). In the interview, the matters at issue were clarified and the Examiner indicated that she would review the teachings of Pinkel. On July 19, 2004, the Examiner left a message with Applicant's representative indicating that she felt she needed to maintain the rejection of the claims for reasons of record. In light of the response submitted herein, Applicants submit that the issues are resolved. If the Examiner has further questions, she is invited to call the undersigned to discuss matters to further prosecution.

II. Rejection Under 35 USC § 112

Claims 20-22, 27-39, 46 and 47 are rejected under 35 USC § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Claims 20, 28, 32-35 and 46 were rejected for depending from non-elected claims. Applicants have amended the claim to remove reference to non-elected claims. Claim 27 was rejected as lacking antecedent

Filing Date: April 6, 1999

support and for being ambiguous. Applicants have amended the claims for technical clarity thereby obviating this rejection. Claim 39 was rejected as lacking antecedent bases. Applicants have amended the claim for technical clarity thereby obviating this rejection. Accordingly, Applicants respectfully request the Examiner to withdraw this rejection.

III. Rejection Under 35 USC § 103

A. Claims 27-39 and 47 are rejected under 35 USC § 103 as being obvious in light of Pinkel (U.S. Patent No. 5,837,196). The Examiner's position appears to be that Pinkel discloses a method of simultaneous measurement of target analytes using a fiber optic array with a plurality of subpopulations of sensor elements, and that Pinkel further discloses a detector system that may be equipped with a computer capable of statistical analysis. The Examiner notes that Pinkel is silent in specifically teaching that the parameters analyzed from the result include the statistical analyses set forth in claims 31, 32, 33, 34, 36, 37 and 39, but alleges that such analyses are standard laboratory practice and that it would have been obvious to one of ordinary skill to use statistical analysis strategies known and conventionally used in chemical and immunological art. Applicants respectfully traverse.

Claim 27 as amended is drawn to a method that includes providing an array with a plurality of subpopulations of sensor elements, wherein subpopulations comprise identical sensor elements, contacting said array with a composition comprising at least a first target analyte, obtaining measurements from said identical sensor elements from at least a first of said plurality of subpopulations and performing a statistical analysis on said measurements from said first of said plurality of subpopulations, whereby statistical validity of said measurements from said identical sensor elements is determined.

Pinkel teaches sensors prepared by bundling individually derivatized optical fibers and methods of detecting target molecules with such individually derivatized optical fiber strands. However, in contrast to the Examiner's assertion, Pinkel fails to teach or suggest methods that include statistical analysis.

As the Examiner is aware, there are three requirements to establish a *prima facie* case of obviousness. These include that "there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations" (MPEP § 2143).

Applicants respectfully submit that Pinkel fails to teach or suggest each element of the claims. Specifically, Pinkel fails to teach or suggest any aspect of statistical analysis as formerly and presently claimed. In the most recent office action the Examiner pointed to several sections of Pinkel as allegedly describing statistical analysis. However, Applicants submit that Pinkel is silent with respect to teaching statistical analysis as claimed.

The Examiner cited column 13, lines 33-56 as teaching statistics. However, Applicants submit that the disclosure at this section is directed to detecting signals not to performing statistical analysis whereby statistical validity of measurements from identical sensor elements is determined. In this regard, Column 13, lines 33-45 set forth that

[t]he detector system may be employed with a computerized data acquisition system and analytical program. In this embodiment, providing a fully automated, computer controlled processing apparatus and measurement

system, the data obtained from the biosensor is processed into immediately useful information. By using such fully automated, computerized apparatus and analytical systems, not only are a variety of different measurements made and diverse parameters measured concurrently within a single fluid sample, but also many different fluid samples may be analyzed individually serially for detection of multiple analytes of interest concurrently--each individual fluid sample following its predecessor in series.

This section is directed to a detector for *measuring* data obtained from the biosensor. Although the section sets forth several different measurements that can be made and parameters that can be measured, there is no teaching or suggestion of performing the claimed statistical analysis. Furthermore, the mere mention of a computerized data acquisition system and analytical program does not compensate for this deficiency because whether or not a computer can be determined in retrospect to be capable of running a particular algorithm does not mean that the algorithm is taught or suggested in the description of the computer itself. More specifically, whether or not the computer of Pinkel is capable of performing Applicants' claimed statistical analysis the art of record provides no motivation to use the computer to perform a statistical analysis whereby statistical validity of measurements from identical sensor elements is determined. Accordingly, in contrast to the Examiner's characterization, this section of Pinkel fails to teach or suggest anything with respect to statistical analysis in general and further fails to describe any of the statistical analyses suggested by the Examiner at p. 6, lines 1-5 of the Office Action mailed April 21, 2004.

In the telephone message of July 19, 2004, the Examiner also suggested that column 16, first full paragraph discussed optimization of assay format or the sensitivities of fiber array configurations and linearity of dynamic ranges. The

Filing Date: April 6, 1999

Examiner appeared to suggest that this was another example of statistical analysis.

Applicants respectfully disagree.

Column 16, first full paragraph recites

[t]o optimize a given assay format one of skill can determine sensitivity of fluorescence detection for different combinations of optical fiber, sensor face configuration, fluorochrome, excitation and emission bands and the like. The sensitivity for detection of analyte by various optical fiber array configurations can be readily determined by, for example, using the biosensor to measure a dilution series of fluorescently labeled analytes. The sensitivity, linearity, and dynamic range achievable from the various combinations of fluorochrome and biosensor can thus be determined. Serial dilutions of pairs of fluorochromes in known relative proportions can also be analyzed to determine the accuracy with which fluorescence ratio measurements reflect actual fluorochrome ratios over the dynamic range permitted by the detectors and biosensor.

However, Applicants submit that while this may describe detection of fluorescence, preparing dilutions of fluorochromes and assay optimization, there is simply no teaching or suggestion of performing statistical analysis whereby statistical validity of measurements from identical sensor elements is determined. More specifically, the description of determining sensitivity achievable from various combinations of fluorochrome and biosensor does not teach or suggest a statistical analysis, much less a statistical analysis whereby statistical validity of measurements from identical sensor elements is determined because there is no description or even suggestion of determining sensitivity based on measurements from *identical* sensors that are then evaluated such that statistical validity measurements are determined. Similarly, there is no teaching or suggestion of determining linearity, dynamic range or

Filing Date: April 6, 1999

fluorochrome ratios based on measurements from *identical* sensors that are then evaluated such that statistical validity measurements are determined

Finally, Applicants note that col. 13, lines 46-56 recite

A variety of in vitro measurements and analytical determinations may be made using a fiber optic biosensor prepared in accordance with the present invention. In vitro applications and assay techniques may be performed concurrently using one or multiple fluid samples. Each concurrently conducted measurement or determination for different analytes of interest is made individually, accurately and precisely. The observed results are then correlated and/or computed to provide precise information regarding a variety of different parameters or ligands individually.

However, there is no teaching or suggestion of performing statistical analysis whereby statistical validity of measurements from a plurality of identical sensor elements is determined. In contrast, this section recites that “[e]ach concurrently conducted measurement or determination for different analytes of interest is made *individually*” (emphasis added). Further, the results in Pinkel are computed to “provide precise information regarding a variety of different parameters or ligands *individually*” (emphasis added).

Accordingly, Applicants submit that Pinkel fails to teach or suggest a method that includes statistical analysis as claimed. Accordingly, a *prima facie* case of obviousness has not been established. Furthermore, the Office has not pointed to any art of record that cures the deficiencies of Pinkel set forth above.

In addition, Applicants note that the Examiner has failed to point to adequate motivation for modifying Pinkel to reach the present claims. The Examiner indicates

Filing Date: April 6, 1999

that it would have been obvious for one of skill in the art to use statistical analysis strategies known and conventionally used in the art. However, Applicants note that valid rejection under 35 U.S.C. § 103 based upon a single prior art reference must be supported by some suggestion of the claimed invention or motivation to reach the claimed invention which is found in that single prior art reference. In re Laskowski, 10 USPQ2d 1397 (CAFC 1989). The disclosure of Pinkel is directed to a sensor and detection methods to obtain "precise information regarding a variety of different parameters or ligands individually". Given Pinkel's focus on making individual determinations and measurements, and the absence of any suggestion of performing statistical analysis whereby statistical validity of measurements from identical sensor elements is determined, as set forth above, Applicants submit that one of skill in the art upon reading Pinkel would not have been motivated to modify Pinkel to reach the present claims, which are directed to methods that include performing a statistical analysis whereby statistical validity of measurements from a *plurality* of identical sensor elements is determined.

Accordingly, Applicants submit that a *prima facie* case of obviousness has not been established. Applicants respectfully request the Examiner to withdraw the rejection.

B. Claims 20, 22 and 47 are rejected under 35 U.S.C. § 103 as being unpatentable over Pinkel et al (US Patent 5,837,196) in view of Stimpson et al. (US Patent 5,559,668).

Pinkel is described above.

Stimpson is directed to a waveguide binding assay method using an array comprising a plurality of light scattering beads for binding with target analytes. The beads are colloidal metals and are dispersed on a substrate.

Application Serial No.: 09/287,573

Express Mail No. ~~EV 298 967 374 US~~

Filing Date: April 6, 1999

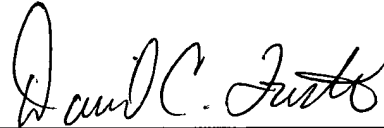
analysis as claimed. Moreover, Sadana fails to cure this deficiency. As noted previously, a *prima facie* case of obviousness requires that each element of the claims is found in the prior art. Applicants respectfully submit that each element of the present claims is not found in the cited references alone or in combination. As such, a *prima facie* case of obviousness has not been established.

CONCLUSION

Please direct further questions in connection with this Application to the undersigned at (415) 781-1989.

Respectfully submitted,
DORSEY & WHITNEY LLP

Dated: July 21, 2004

BY: 

David C. Foster, Reg. No. 44,685 for
Robin M. Silva, Reg. No. 38,304
Filed under 37 C.F.R. § 1.34(a)

Customer Number: 32940
Dorsey & Whitney LLP
Four Embarcadero Center, Suite 3400
San Francisco, CA 94111-4187
Telephone: (415) 781-1989
Facsimile: (415) 398-3249